# STUDIES IN EXPERIMENTAL SCURVY,

## WITH SPECIAL REFERENCE TO THE ANTISCORBUTIC PROPERTIES OF SOME SOUTH AFRICAN FOODSTUFFS.*

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AMONGST South African natives, well-defined scurvy appears to be of rare occurrence so long as they are in their natural environment. When they reach the mines, however, the disease appears to occur frequently, especially since the years of bad local harvests which followed the conclusion of the Boer war. There is little doubt that the explanation of G. Turner with regard to the frequent appearance of scurvy on the Kimberley Mines contains much truth. "Enquiry demonstrated that usually these boys came into hospital about a week after entering the compound. . . . These boys, driven by starvation, came long distances to find work and food. They had been badly fed. The quality of their food, moreover, was bad, consisting practically of store mealies[1]; they could not obtain the milk to which they were accustomed, and the Cape laws prevented them from brewing Kaffir beer. .... The imported mealies these unfortunates had been driven to depend upon were generally artificially dried, and it has been frequently noticed that boys fed on such mealies are particularly prone to scurvy." [11] In the country, however, these are frequently eaten in the green state from the unripe cobs, whereas on the mines only the imported and artificially dried grain is available.

The incidence of scurvy on the mines has been largely reduced by the precaution of a careful medical examination before admission to work, as well as by making additions of fresh meat and vegetables to the diet provided on the compounds. However, in spite of these precautions, occasional outbreaks of scurvy have occurred, and in the year 1920 a marked increase in the number of cases occurring on the Rand showed that further measures were necessary if the disease and consequent loss of efficiency were to be avoided. Further, a number of natives appear to be in a condition of what may be termed latent or incipient scurvy, and this renders them liable to succumb easily to infection and difficult to cure when even simple wounds or abrasions occur. Apparently simple wounds become the sites of ulcers or sores which do not respond readily to treatment, even when the patient has been placed upon a comparatively liberal diet.

The present investigations have been made along the general lines already laid down by Dr. Harriette Chick and other workers at the Lister Institute. Guinea-pigs were used for the most part, but a few experiments were also made with monkeys. The basal diet used was similar to that employed at the Lister Institute,—namely, oats, bran, and fresh milk, autoclaved at a temperature of 120° C. for an hour previous to use. To this basal scorbutic diet was added the substance to be tested, as far as possible in liquid form. Preventive experiments were planned to last about 90 days from the beginning of the special diet. In some cases curative experiments were also carried through, although failure to cure severe scurvy cannot be held to indicate lack of vitamin C in the substance tested.

### *Experiments with Fruit Juices.*

Juices of the following fruits were investigated: peach, pineapple, navel orange, naartje (the local name for the Tangerine orange), and pawpaw (the fruit of *Carica papaya*).

(*a*) *Peach.*—Of seven peach-fed animals, only two were protected from scurvy (Nos. 2 and 5) on average daily rations of 5·8 g. respectively. In No. 5 growth was, however, subnormal and the ridged costochrondral junctions probably indicated a histological condition of a more or less definite scurvy.[10] The appetite of all the animals for milk was good, so that there is no reason to suppose that there was any dietetic deficiency other than that of vitamin C. As the season advanced the peach-juice became less effective and a single animal (No. 57), which had been started on the restricted diet on March 4th, developed scurvy in 32 days on a daily ration of 5 g. of the peach flesh, and made little or no improvement when the ration was trebled in amount. It was found by trial that 260 g. flesh of peach yielded 100 c.cm. of juice and an equivalent ration of juice was therefore substituted for the solid, when necessary, to ensure its consumption.

The results of these experiments indicate that there is a marked falling-off of antiscorbutic value with the advance of the season when only dead-ripe fruit could be obtained.

(*b*) *Pineapple.*—The animals were given 1 c.cm. at first, increasing later to 1·5 c.cm. pineapple juice daily. Symptoms appeared early in the course of the experiment, but the animals survived in a lame condition for the whole experimental period, thus indicating chronic scurvy. Two out of three animals lived in perfect health throughout the experimental period, the third developing an infective complaint. The minimum daily ration of pineapple-juice which affords protection may thus be put at 2·5 c.cm.

Pineapple- and peach-juice are, therefore, about equivalent in antiscorbutic value, but the former is more stable, no sign of deterioration being observed towards the close of the season.

(*c*) *Navel Oranges.*—Experiments with the juice of navel oranges confirm the results already obtained in England by Chick and others, that a minimum protective ration (M.P.R.) of 1·5 c.cm. daily is a sufficient protective ration for a young guinea-pig for a period of about 90 days under the conditions of these experiments.

(*d*) *Naartje* (Tangerine oranges).—Since such closely related fruits as limes (*Citrus medica*, var. *acida*) and lemons (*C. limonum*) have a very different antiscorbutic capacity[7] it seemed desirable to test the vitamin content of naartjes (*Citrus nobilis*, also known as mandarin or Tangerine oranges) which in Africa are often used as substitutes for other oranges. The juice of this fruit seemed not quite as effective as that of the oranges tested, the animals on a ration of 1·5 c.cm. daily developing temporary symptoms suggestive of scurvy in each of three experimental animals, only one of these, however, giving definite signs of scurvy in the post-mortem examination.

(*e*) *Pawpaw* (*Carica papaya*).—Some experiments were started with the juice of the pawpaw. These are being continued by Dr. B. D. Pullinger at the South African Institute for Medical Research. This is perhaps one of the best fruit-juices for the cure of severe cases of experimental scurvy, especially in cases of scorbutic dysentery, when juices such as tomato, orange, or cabbage are apt not to check the dysentery. The M.P.R. for a young guinea-pig appears to be about 5 c.cm. daily, but further evidence is required on this point.† Pawpaw would probably be of much value as a safe source of fruit-juice for hand-fed infants in hot climates. It is, moreover, plentiful in certain localities although not at present a very cheap fruit.

In considering the relative values of these fruits, not only the value of the juice but also the yield, and the amount of waste must be considered. Some idea of their comparative antiscorbutic values is given in Table I.

TABLE I.—*Comparative Values of Peach, Pineapple, Orange, Naartje, and Pawpaw Fruits.*

| Fruit. | M.P.R. (c.cm.) | Weight whole fruit (g.) corresponding to M.P.R. | Relative anti-scorbutic value. |
|---|---|---|---|
| Peach .. .. | 2–3 (in season) | 5–8 (flesh only) | 50–80 |
| Pineapple .. .. | 2·5 | 9 | 44 |
| Orange (navel) .. | 1·5 | 4 | 100 |
| Naartje .. .. | 1·5 | 5 | 80 |
| Pawpaw .. .. | 5·0 | 10 | 40 |

It may be estimated that the flesh of peach and pineapple, weight for weight, therefore, are about equally valuable for the prevention of scurvy, whilst oranges are twice as valuable as either. Peaches being more variable in their value are unsatisfactory as a sole source of antiscorbutic vitamin.

### *Experiments with Vegetable Juices.*

The following vegetable-juices were investigated: vegetable marrow, pumpkin, sweet potatoes, and sugar cane. In the first three cases the vegetables were first scraped on a kitchen grater, when the débris was

* An abstract of a report of an investigation into the relative antiscorbutic values of the foodstuffs commonly in use in the dietary of native workers on the Rand Mines, carried out at the South African Institute for Medical Research, Johannesburg.

† Later information from Dr. Pullinger confirms this estimate.

pressed by hand through mosquito-netting to obtain the juice. The sticks of sugar cane were first peeled, then cut into short lengths, passed through a mincing machine, and the products squeezed as before. The sugar cane was received fresh weekly from the Illovo Sugar Estates through the kindness of Mr. W. Pearce.

(*a*) *Vegetable Marrow.*—The results were not conclusive, but it seemed clear that the juice of the young green marrow was more powerfully antiscorbutic than that at the end of the season, when doubling or even trebling the dose of the juice had no ameliorative effects on scorbutic animals. Out of nine animals placed on experiment, only one survived with good health until near the end of the experiment, when this, too, developed definite symptoms of scurvy. The average ration of this animal was 7·5 c.cm. Owing to the short season of the vegetable marrow in this locality, it was not possible to develop these experiments further.

(*b*) *Pumpkin.*—With pumpkin-juice also, protection was only gained with high rations of the expressed juice, as much as 15 c.cm. being required. Two animals on this ration were fine, well developed, and showed only a trace of scurvy when examined after death. The M.P.R. of this juice therefore was about 15–20 c.cm. daily.

(*c*) *Sweet Potato.*—Sweet potatoes (*Ipomea batatas*) are a common vegetable in this country and form a favourite article of diet with the natives. According to Hand and Cockerham[6] they are, weight for weight, of greater food value than the so-called Irish potato (*Solanum tuberosum*). This appears to be partly due to their greater proportion of solid matter, and partly to the presence of proteins in the form of albuminoids instead of in the form of amides, as in the Irish potato. Guinea-pigs will not readily eat the flesh of either kind of potato, but they drink the raw expressed juice willingly. Symptoms of severe scurvy were produced in each of two animals given 3 c.cm. of this juice daily; but all animals given as much as 5 c.cm. were afforded complete protection. The M.P.R. is therefore between 4 and 5 c.cm. daily, and is probably nearer to the upper of these two amounts. Sweet potato is a convenient source of antiscorbutic food for those unable to obtain the more expensive green vegetables and fruit, but it must be remembered that in cooking there will be a loss of antiscorbutic value of at least half and probably more than this.[3] Preventive rations should be calculated to allow for this loss. Table II. shows the relative values of these vegetables when raw with respect to vitamin C.

TABLE II.—*Comparative Values of Pumpkin, Vegetable Marrow, and Sweet Potato.*

| Vegetable. | M.P.R. (c.cm.) | Weight (g.) raw vegetable required to give M.P.R. | Relative anti-scorbutic value. |
|---|---|---|---|
| Pumpkin .. .. | 15–20 | 75–100 | 5 |
| Vegetable marrow | 5 (young) | 12 (young) | 33 |
| | >15 (mature) | 37 (mature) | 11 |
| Sweet potato .. | 5 | 13 | 31 |
| Navel orange (see Table I.).. .. | 1·5 (in season) | 4 | 100 |

(*d*) *Sugar Cane.*—No antiscorbutic value could be detected in the fresh juice of the sugar cane, but rations higher than 10 c.cm. daily seemed not to be tolerated by the animals, which rapidly became extremely ill. Moreover, one out of three guinea-pigs fed with 10 c.cm. of sugar-cane juice with a full ration of orange juice actually showed symptoms of scurvy; whereas all three were in bad condition compared with those given orange juice without excess of carbohydrate.

*Germinating Seeds (Cow Peas, Soya Beans, Kaffir Corn).*

The cow-peas used were two varieties commonly supplied as food for the native workers on the mines (*Vignum sinense*, var. Whip-poor-Will and var. Wonder). After soaking in water, they germinated readily at a temp. of 25–30° C. As in previous experiments with "Clipper" peas in England, a ration of 2·5 g. raw germinating cow-peas was found sufficient to protect from scurvy for nearly 90 days; Soya beans (*Glycine hispida*), however, when germinated had no perceptible antiscorbutic value when treated in the same way. This unexpected result may be connected with the fact that these seeds store oil, instead of starch, as do the cow-pea and most other leguminous seeds.

In the case of raw germinating Kaffir corn, there was great difficulty in inducing the animals to eat sufficient of the corn regularly. Three animals which each took daily 5 g. of the pulp had marked symptoms of scurvy within 33 days from the beginning of the experiment, but survived in a scorbutic and lame condition until the end of the experimental period. Two others which received a ration of 10 and 12 g. respectively also developed symptoms at nearly the same stage. Towards the end of the experiment these were given also a ration of orange-juice (1 c.cm.) on alternate days. This small addition was sufficient to cure the scurvy symptoms observed. The deficit in antiscorbutic on these rations was therefore not great; no attempt was made, however, to feed larger rations on account of the labour involved in the daily hand feeding, which was the only method to ensure the consumption of so much Kaffir corn.

*Pulses and Cereals.*

The difference in the antiscorbutic value of pulses and cereals in the germinating state is of interest in connexion with the structure of the seeds. In the former case the seed is occupied entirely by the embryo; in the latter with a food reserve or endosperm, the embryo plant occupying only a small part of the bulk of the seed. The suggestion obviously is that the embryo alone is responsible for the synthesis of the antiscorbutic vitamin during the process of germination.

*Methods of Cooking Germinated Pulses.*

In previous experiments it has been shown that boiling germinated lentils for only 15 minutes destroyed about four-fifths of their antiscorbutic value.[2] Lentils soften in cooking more easily than either peas, beans, or cow-peas. In addition, at the high altitude of the Rand the boiling point (94·5° C.) of water makes it necessary to boil cow-peas for at least an hour and a half in order to soften them sufficiently. Other methods were therefore tried in the attempt to soften the peas with the minimum loss of vitamin value.

(*a*) *Boiling.*—In one group of experiments the cow-peas were thrown into excess of boiling water to which ammonium carbonate in the proportion of 0·5 g. per litre was immediately added.[9] They were then boiled for 20 minutes, when they were about as soft as they would have been after boiling in water alone for an hour. The time of cooking was reckoned from the time at which the water boiled again after the addition of the seeds. Parallel experiments were started at a later date with cow-peas cooked for only five minutes both with and without ammonium carbonate. The results of these experiments show that a great part of the destruction in cooking occurs in the first few minutes and before any appreciable softening of the tissues. As far as could be seen from the small numbers of animals used on experiment, there seemed to be a distinctly better result with the animals which had the cow-peas cooked for five minutes without than those with the ammonium carbonate. With longer cooking, however, the increased destruction of vitamin C is greater than that produced by adding enough ammonium carbonate to reduce the time needed from one and a half hours to 20 minutes. In all cases protection was achieved only when large rations (from 15–20 g.) were given daily. In one case much improvement was seen by merely decreasing the time of cooking from 20 minutes to 5 minutes. This was manifest almost at once, in a better appetite, an increased weight, as well as later in abatement of the symptoms of scurvy.

(*b*) *Steamed over Water.*—1. Over water to which ammonium carbonate had been added. It was found necessary to steam for half an hour in order to soften the peas sufficiently. A ration of 10 g. produced scurvy of a mild but definite type. On the whole this was a satisfactory way of cooking and probably involved the least loss by diffusion into the water. 2. In an autoclave for 10 minutes at 105–110 lb. pressure. Contrary to expectation, although the method was satisfactory so far as softening and flavour was concerned, the animals did not do well on this method, and severe scurvy resulted after rations of 10–20 g. had been adopted.

(*c*) *Simmered 20 Minutes in Water with the Addition of Ammonium Carbonate.*—In this method the cow-peas were thrown into just enough water to cover them and were then simmered slowly at a temperature of 90–95° C. after adding ammonium carbonate in proportion of 0·5 g. to 100 c.cm. of water. As the cooking proceeded a thick brownish juice was formed, and this was poured off separately and fed to the animals in amount proportional to their ration. These were the most satisfactory of all the animals and were fine, strong, and well grown when the experiment terminated. The rations were, however, high. An original ration of 10 g. being found insufficient, it was increased to 20 g. daily. The

average ration in each of three animals was 17 g., and their condition was markedly better than those having the same average amount of the boiled cow-peas without the addition of any juice. It is probably significant that these were also the most easily fed and took their high rations with the least forcing. There is little doubt that the juice contains an appreciable vitamin value, containing presumably both the water soluble vitamins.

On the whole, therefore, it was recommended that the best method of cooking germinating cow-peas was either to steam in a chamber over water to which a small proportion of ammonium carbonate had been added (0·5 g. to a litre), or preferably, to simmer in a small quantity of water in a double cooker, the ammonium carbonate being added to the water as the peas are thrown in, and the cooking water being eaten as well as the peas themselves. It is probable that on a large scale some modification in the time of simmering and in the proportion of ammonium carbonate might be found advantageous; but (1) the carbonate should not be sufficient to affect the flavour of the peas or to make them slimy, and (2) the juice should be well stirred around the peas and served with each ration.

*Experiments with Kaffir Beer.*

In South Africa there is a widespread belief in the value of some kinds of native beer, especially as an antiscorbutic drink. Owing to the dangers of intoxication, the Cape laws forbid the brewing of this drink except in certain cases, when it is provided freshly brewed and with a very low alcoholic strength (2–3 per cent.). Natives working on the Rand mines are allowed a liberal ration of this beer twice or three times a week. There are a variety of ways of making the beverage, but in all cases the malt used is made from sprouted Kaffir corn (*Sorghum vulgare*), and it is allowed to ferment in a brew with the addition of mealie meal (i.e., maize meal) for not more than 24 hours before issue. Samples of the freshly brewed beer were obtained regularly from two different mine compounds and a number of feeding experiments with guinea-pigs were started.

In no case was it found possible to secure protection from scurvy in guinea-pigs by means of a ration of Kaffir beer. This was not surprising, however, as the animals would not take the beer readily, an together with their basal milk ration it was impossible to feed into them sufficient even to approach the protective amount. In a few experiments the beer ration was supplemented with a small ration of orange-juice, in itself too little to give protection. The additive effect of both the rations was then sufficient to give the required protection.

Further results were sought by the use of monkeys. Two monkeys were induced to drink a daily ration of at first 80 c.cm. and later 200 c.cm. of the beer, and were kept on an otherwise scorbutic diet. The basal diet was mainly brown bread, butter, cheese, pea-nuts, and autoclaved milk ad libitum. The Kaffir beer ration was fed at first mixed with autoclaved milk, and was given by hand. The experiments were started in April, 1921, and were not complete at the time of writing the report. They have been concluded under the supervision of Dr. B. D. Pullinger, whose results confirm those mentioned below.

The initial weight of the monkeys was 3610 and 3770 g. respectively. (Table III.) After 3½ months of experiment No. III. died after a few days' illness of some apparently intestinal infection. No sign of scurvy was found at the post-mortem, with the exception of local well marked hæmorrhage in the subcutaneous tissue of the right shoulder. No tenderness of the limbs had been observed during life, though a certain stiffness in movement on taking exercise had been noticed and had been attributed to the enforced confinement. No. I., on the other hand, received the same diet for four months without any sign of the development of scurvy until the 114th day, when her gums were obviously purple and swollen. Her average ration of Kaffir beer during this time was 85 c.cm. daily. This ration seems to have about the same effect as a ration of 75 c.cm. fresh English milk given by Hume to monkey "Diana" at the Lister Institute,[1] the monkey developing scurvy after 119 days.

TABLE III.—*Average Daily Consumption of Kaffir Beer (K.B.) and Autoclaved Milk (A.M.)*

| Monkey No. | — | Daily average in c.cm. during months of experiment. | | | | Average in c.cm. for first four months. | Initial body weight in grammes. |
|---|---|---|---|---|---|---|---|
| | | 1st | 2nd | 3rd | 4th | | |
| I. .. | K.B. | 49 | 77 | 110 | 103 | 85 | 3610 |
| | A.M. | 146 | 226 | 260 | 279 | 237 | — |
| III. .. | K.B. | 62 | 174 | 228 | 224* | 166 | 3770 |
| | A.M. | 189 | 344 | 334 | 324* | 295 | (4320 g.) final weight |

* Two weeks only.

There is thus every reason to think that Kaffir beer is possessed of some small antiscorbutic value; and when forming a large part of the daily beverage taken by a Kaffir who would otherwise receive but a small proportion of antiscorbutic food, it is probably an important factor in keeping him in health. The fact that this drink is much appreciated by the native is also a factor of some importance in arranging a native dietary.

The beer thus tested was received from the Ferreira Deep Mine, and the preparation was described by the compound manager thus:—

"Equal quantities of Kaffir corn malt and mealie meal are put into hot water and cooked about five minutes. . . . . It is then cooked in our ordinary steam pots for three hours, put into barrels, and left cooling for a further two and a half days. We then add about two and a half buckets—i.e. 30 lb.—Kaffir corn malt per barrel (45 gallons), and after leaving for 2 to 4 hours the stuff is sieved and served."

In other compounds the proportion of malt is reduced, the mealie meal being increased, and the time of standing to ferment being proportionally longer. Only one sample of beer prepared by such a method was tested and gave appreciably worse results with guinea-pigs. It therefore appears that it is the proportion of malt added rather than the time of fermentation which gives the slight but appreciable anti-scurvy value of the drink.

*Curative Experiments.*

A number of experiments were undertaken with a view to curing cases of more or less pronounced scurvy. It is impossible to discuss these in the present communication, but the following facts, amongst others, were noticed. Orange-juice here, as often previously, was found to be of marked curative power. Tomato-juice, which has been especially recommended for this purpose in America, was not found to be of any appreciable value. (Recent experiments by Dr. Pullinger indicate that later in the season the juice of the tomato was much thicker, and was as effective as orange-juice both in preventing and in curing scurvy. This is a striking confirmation of the work of A. F. Hess as to the variable nature of certain vegetable and fruit juices with respect to the content of vitamin C.[8]) Pawpaw-juice was found to have unexpectedly good effects, especially in cases of severe scurvy accompanied by scorbutic dysentery. The appetite improved, the diarrhœa ceased, and the animal put on weight in a surprisingly short time. Further experiments by Dr. Pullinger are in progress on the vitamin value of this juice. In addition to the above investigations, a number of tests were made of certain commercial preparations received during the course of the experiments.

*The Local Problem.*

In discussing the bearing of the results of these experiments on the local problem of the occurrence of scurvy (latent or otherwise) among the natives on the Rand mines, the suggestion is obvious that the vitamin content of the diet should be maintained at a somewhat higher level that heretofore, in order to prevent the occurrence of the disease. So far as the

vitamin C is concerned, this can be done cheaply and effectively by giving a regular ration either of fruit, such as oranges, pineapples, and naartjes when these are in season, or of vegetables such as sweet potatoes, when the former are not available. In the latter case, it is important to see that the rations are not given *after too long cooking*.[4] Some additional protection may be given by means of the Kaffir beer ration as made at the Ferreira Deep Mine. Previous germination of the cow-peas, or beans, used in the daily ration will also help, but these should be cooked as little as possible, and if cooked with little water, should be served with their liquor. When a vegetable such as pumpkin (a favourite with the native) is given, either a much larger ration should be allowed or the antiscorbutic element in the diet should be supplemented in some other way. As a matter of fact, since the scale adopted under the Native Regulation Act, December, 1920, embodying improvements in substantial accordance with the above suggestions, cases of scurvy have been of rare occurrence.

A further problem dealt with is the possibility that there may be more than one vitamin deficiency in the diet. This appears very probable in certain cases, and marked improvement is brought about by the administrations of food or preparations containing vitamins A or B. Certain cases recorded among the experimental animals throw some little light upon this problem. The relation of the energy value of the diet to the vitamin need is also discussed.

TABLE IV.—*Food Products Tested at South African Institute for Medical Research, Jan.-Sept., 1921.*

| Fresh juice of— | Minimum dose protective against experimental scurvy in guinea-pigs. | Approx. value "C." |
|---|---|---|
| Orange (navel) | 1–1·5 c.cm. | + + + |
| Naartje | 3 c.cm. | + + |
| Pineapple | 2·5 c.cm. | + + |
| Peach | 3 c.cm. (in season) | + |
| | >5 c.cm. (end of season) | L.v. |
| Pumpkin | 15–20 c.cm. | ,, |
| Vegetable marrow | 5 c.cm. (green and young) | + |
| | >15 c.cm. (ripe and old) | L.i.a.v. |
| Sugar cane | 10 c.cm. (no protection whatever) | ,, |
| Sweet potato | 5 c.cm. | + |
| Fresh green mealies | 15–20 g. | + |
| Fresh germinating Kaffir corn | >12 g. (probably 15–20 g.) | + |
| Dry malted germinating Kaffir corn | >10 g. (no protection whatever) | L.i.a.v. |
| Fresh raw germinating cow-peas (var., Whip poor Will) | 2·5 g. | + + |
| Fresh raw germinating cow-peas (steamed 30 min.) | 15 g. or more. | + |
| Fresh raw germinating cow-peas (boiled 20 min.) | 16 g. (very little protection) | L.v. |
| Fresh raw germinating cow-peas (simmered in little water 20 min.) | 16 g. | + |
| Kaffir beer — Crown Mines | >10 c.cm. | L.v. |
| Kaffir beer — Ferreira | >10 c.cm. | L.v.* |

L.v. = Little value. L.i.a.v. = Little if any value.
* But better than from Crown Mines; comparable with value of fresh cow's milk.

The dietary of native mine-workers as at present enforced is detailed, and a table is given of the principal foodstuffs hitherto tested with regard to the vitamins A, B, and C, reproduced above as Table IV.

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# ON BLOOD GROUPING AND ITS CLINICAL APPLICATIONS:

## WITH A SIMPLE METHOD OF GROUP DETERMINATION.

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AT the present time the principal practical importance attaching to the allotting of blood from human beings to its appropriate group lies in the field of transfusion. That transference of blood from a healthy to an anæmic subject should be a desirable procedure is so obvious that it is difficult to say that the suggestion originated with any one particular person. At first difficulties in technique of transfusion barred the way to its wide application, but these having been overcome—as they were very thoroughly overcome during the war—it became evident that, whereas in most instances marked benefit followed a blood transfusion, in some few the reverse was most strikingly the case. In this latter class of case death sometimes followed immediately upon the introduction of the fresh blood from a healthy subject, while in others, although death did not immediately result, symptoms such as rigors, hæmoglobinuria, loss of consciousness, and a condition of "shock" rendered the condition of the patient considerably worse than it was before recourse was had to transfusion.

### *Occasional Incompatibility of Blood.*

The occurrence of these symptoms after transfusion led to the realisation that some human bloods were incompatible with others; investigations conducted by many surgeons practising transfusion finally established the fact that evil results followed the procedure in those cases, and in those only, where the serum of the recipient was capable of agglutinating the red cells of the donor. It has long been recognised[1 2] that the serum of certain human bloods has the power of agglutinating red cells from other individuals. This phenomenon, first noted in the serum of sufferers from various diseases, was thought to be an abnormality resulting from and peculiar to the disease. Later it was established by the work of Moss,[3] von Dungern and Hirschfeld,[4] Jansky,[5] and Landsteiner,[6] that agglutination of red cells might be brought about by serum from perfectly normal individuals. As a result of the work of these observers, it finally became possible to place all human bloods into four groups, according to the manner in which their red cells and serums interacted with each other; the manner of this interaction was elucidated by von Dungern and Hirschfeld.

### *Factors of the Four Groups.*

These authors postulated two agglutinable substances resident in the corpuscles and two corresponding agglutinins resident in the serums. The agglutinable bodies in the red cells they denominated A and B respectively and the agglutinins capable of acting on them *a* and *b*. They further postulated that the agglutinin capable of acting upon the agglutinable body present in any given red cell will never be normally present in the serum of the blood containing that red cell, and conversely that the agglutinin opposite in sign to that of the red cells in the blood will always be present in the serum of that blood. On this basis they allotted the agglutinins and agglutinable factors in the serums and red cells of the four blood groups as follows:—

| *Group.* | *Serum.* | *Corpuscles.* |
|---|---|---|
| I. | Agglutinin nil | Agglutinable factor A and B. |
| II. | ,, *b* | ,, ,, A. |
| III. | ,, *a* | ,, ,, B. |
| IV. | ,, *a* and *b* | ,, ,, nil. |

Absorption of serums and corpuscles of the various groups against each other has, in the hands of various observers,[7 8 9] established the correctness of this view.